

REMARKS

Claims 11, 12, 16, 22-27, 32-34, 44, 50-54, 56, 58-69, 73-81 and 83-109 are pending and under examination. Claims 16, 25, 27, 34, 44, 67, 76, 78, 81 and 83 have been amended. Support for the amendments can be found in the specification as filed, for example, on page 25, lines 17-31, and page 33, Table 1. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Rejection Under 35 U.S.C. § 102

Claims 11, 16, 22, 24-27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 73, 75-79, 81, 83-86, 88, 89, 91-92, 94-95, 97-98, 101, 103, 105, 107, and 109 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Turner et al., Breast Cancer Res. Treatment 46:69 (1997). As in the previous Office Action, the Office maintains that “. . . because DCIS is a breast cancer with no lymph node involvement, the DCIS reads on the instant stage I, and stage II with no lymph node involvement. Therefore, Turner et al. teach all limitations of the claims.” See Office Action dated January 29, 2008, page 4, first paragraph and the present Office Action dated October 15, 2008, page 3, last sentence to page 4, line 1. Applicant respectfully maintains, for the reasons of record, that Turner et al. does not anticipate the claimed methods.

Independent claims 16, 25, 27, 34 and 44, which recite stage I of breast cancer, have been amended to recite “in which the cancer is infiltrating [invasive] but has no lymph node involvement.” Independent claims 67, 76, 78, 81 and 83, which recite stage II of breast cancer, have been amended to recite “in which the cancer is infiltrating [invasive] but has spread no further than the lymph nodes local to breast.” As amended, claims 11, 16, 22, 24-27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 73, 75-79, 81, 83-86, 88, 89, 91-92, 94-95, 97-98, 101, 103, 105, 107, and 109 do not read on Turner et al. and are not anticipated. Applicant respectfully requests that this rejection be withdrawn.

The above claim amendments, without prejudice, provide definitions of stages I and II of breast cancer to differentiate these stages from that of DCIS. Applicant maintains the position of record that DCIS, stage I and stage II are distinct stages of breast cancer well known in the art. Applicant further submits that in DCIS, breast cancer cells are *in situ* (Latin for ‘in its place’), that is, confined to the ducts of the breast, whereas in stages I and II, breast cancer cells are

invasive and have spread beyond the *in situ* stage and into the breast tissues (see Exhibit 2 submitted with response filed July 23, 2008). Accordingly and in light of the evidence of record and the explicit recitation in the claims of the meaning of stage I and stage II breast cancer that clearly distinguishes from DCIS, Applicant maintains that the claims do not read on Turner et al. and are not anticipated. Applicant respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 11, 12, 16, 22, 24-27, 32-34, 44, 50-53, 56, 58-61, 67-69, 73, 75-81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98, and 100-109 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Sano et al., U.S. Patent No. 5,665,539, is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that the claimed methods are unobvious over Turner et al., alone or in combination with Sano et al.

As discussed above and for the reasons of record, Turner et al. neither teaches nor suggests the claimed methods relating to stage I or stage II of breast cancer. Sano et al. does not cure this defect, as it contains no teaching or suggestions that would complement the teaching of Turner et al. with regard to stage I or stage II of breast cancer.

The Office contends that “[w]hile Turner et al. do not explicitly disclose the stage of the invasive breast carcinoma used in their study, detecting BAG-1 in non-invasive and invasive breast carcinoma of stages I-IV using the methods of Turner et al. would have been obvious to one skilled in the art in view of the teachings of Turner et al.” Office Action page 5, first paragraph. Applicant respectfully traverses.

Applicant submits that the present invention is based on the discovery that BAG-1’s expression significantly correlates to survival in early-stage of breast cancer patients, that is, those having stage I and II breast cancer. While Turner et al., in lines 13-16 of their abstract, disclosed that “10-year OS [overall survival] and DDFS [distant disease free survival] for patients with overexpression of cytoplasmic BAG-1 in IC [invasive carcinoma] specimens was 75% and 70%, respectively, as compared with 62% and 35% for tumors with low cytoplasmic BAG-1 levels (p=0.06),” Applicant in the present invention discovered that 10-year OS and DMFS (distant metastasis-free survival) for patients with overexpression of BAG-1 protein in

stages I and II of breast cancer was 90% and 84%, respectively, as compared with 40% and 40% for those with low BAG-1 levels ($p < 0.001$) (see page 35 of the application as filed, lines 5-14, and Figure 1).

In other words, Turner et al. had showed that BAG-1 overexpression correlated with an overall survival rate of 75% while BAG-1 under-expression (or low levels) correlated with an overall survival rate of 62%. A skilled artisan working in the cancer field would have understood that this relatively small differential in overall survival rate between specimen over- or under-expressing BAG-1 with $p = 0.06$ is not significant enough to conclusively suggest that BAG-1 can be a reliable diagnostic tool for predicting survival, let alone being a diagnostic tool for predicting survival of patients with stage I or stage II of breast cancer. Indeed, Dr. Reed, a renowned expert in the field of cancer had attested to this fact (see Reed Declaration submitted previously as Exhibit 2 with response filed December 13, 2006).

Contrary to the findings of Turner et al., Applicant discovered and disclosed in the specification that, at stages I and II of breast cancer, BAG-1 overexpression correlates with 90% overall survival rate while BAG-1 under-expression correlates with 40% overall survival rate with $p < 0.001$ (see page 35, lines 5-14). This significant correlation of BAG-1 expression with 90% overall survival demonstrated by the large gap between the two survival rates and the small p-value is a result no ordinary person of skill in art could have predicted based on the teachings of Turner et al., alone or in combination with Sano et al. Moreover, such a high survival rate (90% vs. 40%) would be considered very significant in the field of cancer, which has such a high potential for mortality.

Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in combination with Sano et al. Accordingly, Applicant respectfully requests withdrawal of this rejection.

The rejection of claims 11, 16, 22, 24-27, 32, 34, 44, 50-54, 56, 58-68, 73, 75-79, 81, 83-99 and 100-109 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Sauter et al., Br. J. Cancer 76:494-501 (1997), is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that the claimed methods are unobvious over Turner et al., alone or in combination with Sauter et al.

As discussed above and for the reasons of record, Applicant respectfully maintains that Turner et al. does not teach or suggest the claimed methods relating to stage I and stage II of breast cancer. Furthermore, Applicant respectfully maintains that Sauter et al. does not cure the deficiencies of Turner et al. in teaching stage I and stage of breast cancer. Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in combination with Sauter et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 11, 16, 22-27, 32, 34, 44, 50-54, 56, 58-61, 67, 68, 73-79, 81, 83-86, 88, 89, 91, 92, 94, 95, 97, 98 and 100-109 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Takayama et al., Cancer Res. 58:3116-3131 (1998), is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that the claimed methods are unobvious over Turner et al., alone or in combination with Takayama et al.

As discussed above and for the reasons of record, Applicant respectfully maintains that Turner et al. does not teach or suggest the claimed methods relating to stage I and stage II of breast cancer. Furthermore, Applicant respectfully maintains that Takayama et al. does not cure the deficiencies of Turner et al. in teaching stage I and stage II of breast cancer. Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in combination with Takayama et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 11, 16, 22, 24-27, 32, 34, 44, 50-54, 56, 58-68, 73, 75-79, 81, 83-99 and 100-109 under 35 U.S.C. § 103 as allegedly obvious over Turner et al., *supra*, in view of Love, U.S. Patent No. 6,221,622, is respectfully traversed. Applicant respectfully maintains, for the reasons of record, that the claimed methods are unobvious over Turner et al., alone or in combination with Love.

As discussed above and for the reasons of record, Applicant respectfully maintains that Turner et al. does not teach or suggest the claimed methods relating to stage I and stage II of breast cancer. Furthermore, Applicant respectfully maintains that Love does not cure the deficiencies of Turner et al. in teaching stage I and stage II of breast cancer. Applicant respectfully maintains that the claimed methods are unobvious over Turner et al., alone or in

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combination with Love. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

In view of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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